Spinal anaesthesia in neonates and infants: what about the cerebral oxygen saturation?

C. Sola1,*, L. Hertz2, S. Bringuer2, P. De La Arena1, C. Macq1, S. Deziel-Malouin1,3, O. Raux1 and C. Dadure1

1Department of Anaesthesia and Critical Care Medicine, Paediatric Anaesthesia Unit, Lapeyronie University Hospital, Montpellier, France, 2Biostatistics and Clinical Research Consultant, Department of Anaesthesiology and Critical Care Medicine, Lapeyronie University Hospital, Montpellier, France and 3Department of Anesthesia, Sherbrooke University Hospital, Sherbrooke, Canada

*Corresponding author. E-mail: c-sola@chu-montpellier.fr

Abstract

Background. Spinal Anaesthesia (SA) has been firmly established as an efficient and safe technique, with minimal cardio-respiratory disturbance when administered in the neonatal period. Our objective was to assess the haemodynamic consequences of SA in infants, particularly its impact on cerebral perfusion using near-infrared spectroscopy (NIRS)-based cerebral oximetry (rSCo2).

Methods. All infants up to 60 weeks’ postmenstrual age, whether formerly preterm or not, and undergoing spinal anaesthesia, were enrolled. Haemodynamic data records, rSCo2 and mean arterial blood pressure (MAP), were prospectively collected before SA (T0) and every five min for 30 min (T30) after the puncture. Compared with baseline measures, any changes of >10% in rSCo2 and of >20% in MAP were considered clinically significant. Relative variations of data between T0 and T30 were analysed.

Results. Data of 103 infants were analysed. The mean relative changes in rSCo2 were 2.25% (97.5% CI [3.97; –0.5]) at T15, and 0.11% (97.5% CI [1.67; 1.90]) at T30. No significant variation of rSCo2 was recorded. The mean changes in MAP were respectively –13.94% (97.5% CI [–17.74; –10.14]) at T15 and –20.27% (97.5% CI [–24.25; –16.29]) at T30. MAP decrease was statistically and clinically significant 30 min after SA. No correlation between changes in MAP and rSCo2 was found. The subgroup analysis did not reveal any effect of added intrathecal clonidine or preterm birth history on these results.

Conclusions. In neonate and infants, SA did not cause clinically significant variation in cerebral oxygen saturation. Despite a significant decrease in MAP, cerebral auto-regulation seems to remain effective in neonates and not altered by spinal anaesthesia.

Key words: anaesthesia, spinal; blood pressure; cerebral auto-regulation; infants; near-infrared; neonates; spectroscopy

With the constant progress of neonatal management, perioperative outcomes have been largely improved. Nevertheless, anaesthesia and surgery-related morbidity and mortality are higher in infants than older children and adults. Reduction of neurologic complications related to perioperative stress is imperative for the anaesthetic care of the newborn. Ensuring the maintenance of tissue perfusion pressure, particularly an optimal cerebral oxygenation is an on-going challenge that cannot be achieved without filling some of our knowledge gaps on basic neonatal pharmacology and physiology. A recent review on neonate cerebral auto-regulation (CA) highlighted the links between perioperative stress and postoperative neurocognitive outcome.
Editor’s key points

• Spinal anaesthesia is used in neonates requiring surgery, but decreases heart rate and blood pressure.
• Systemic hypotension may cause cerebral ischaemia, particularly if cerebral autoregulation is impaired.
• The authors assessed regional cerebral oxygenation in a cohort of children undergoing spinal anaesthesia.
• Although the heart rate systemic blood pressure fell significantly, there was no significant change in cerebral oxygenation.

In addition, many experimental and clinical studies support the current concerns about a possible direct and/or indirect neurotoxicity related to anaesthesia on the developing brain: the assumed direct toxicity of anaesthetic agents and the intrinsic effects of anaesthesia on systemic parameters such as blood pressure (BP), glycaemic index, temperature, acid-base balance and hyper or hypoxia, could potentially cause an alteration in the quality of cerebral blood flow (CBF). Furthermore, especially in situations of homeostatic instability, monitoring of systemic BP probably does not provide sufficient information to ensure adequacy between cardiac output and tissue oxygen requirements.

Near-Infrared Spectroscopy (NIRS) represents currently a relevant tool to detect cerebral ischaemia described for the first time in 1977, this non-invasive continuous monitor of tissue oxygenation provides a real-time view on the oxygenation state of brain tissue, by measuring the regional cerebral oxygen saturation $\left( S_cO_2 \right)$. A decrease greater than 20% of baseline $S_cO_2$ has been associated with a significant increase in neurological perioperative complications. On the other hand, a reduction of less than 13% compared with the $S_cO_2$ reference value appears to guarantee the absence of severe cerebral ischaemia. Thus, in stable respiratory conditions, a decrease in the cerebral saturation greater than 10% can be interpreted as a warning threshold of an imbalance between oxygen supply and requirements of cerebral metabolism.

In infants up to 60 weeks’ postmenstrual age (PMA), spinal anaesthesia (SA) has been firmly established as an efficient and safe alternative to general anaesthesia (GA), with minimal cardiac-respiratory disturbance, including during the neonatal period. In contrast, Bonnet and colleagues reported a significant decrease in mean arterial blood pressure (MAP) associated with a decrease in the CBF measured by trans-cranial Doppler (TCD), at 5 and 10 min after SA, in 12 prematurely born infants. The authors concluded that there could be an absence of effective CA in former preterm and expressed concerns about the potential risks of hypotension related to the SA on the neurological outcome of neonates.

The purpose of this study was to assess the haemodynamic consequences of SA in infants, particularly the impact on cerebral perfusion using near-infrared spectroscopy (NIRS)-based cerebral oximetry ($S_cO_2$). Our hypothesis was that spinal anaesthesia performed in neonates and infants does not lead to significant changes in $S_cO_2$.

**Methods**

This prospective observational study was conducted in the Department of Paediatric Anaesthesia of Montpellier University Hospital. Institutional Review Board was obtained from the French Society of Neonatology (SFN - n° 1401). Over the course of two yr, all infants younger than 60-weeks’ PMA, born prematurely or not, scheduled to benefit from a SA for a sub-umbilical surgery with an expected duration of less than 90 min, were eligible. The parental informed consent was obtained at the time of preoperative anaesthesia consultation. Exclusion criteria were the presence of local or systemic infections, bleeding disorders, vertebral malformations, or parental refusal.

All patients received premedication with 20 mg kg$^{-1}$ of intravenous atropine (Aguettant Lyon, France) thirty min before transfer to operative room and the application of a local anaesthetic cream (EMLA 5% cream, Astra Zeneca, Russel-Malmoison, France) on the area planned for puncture. No sedative agent (particularly benzodiazepine) was administered at premedication time. In the operating room, standard monitoring, including BP, heart rate (HR), pulse oximetry ($Sp_O_2$) and skin temperature sensor, were applied and measures taken to prevent hypothermia. For intraoperative fluid and electrolyte management, Ringer’s lactate - 1% dextrose - solution was administered (B66°, AP-HF, Paris, France) according to the Berry recommendations. SA was performed in strict aseptic conditions with a 25-G needle, Quincke Bevel, 30 mm length (Vygon, Ecouen, France), at the L3-L4 or L4-L5 intervertebral space. Spinal anaesthesia was induced with 1 mg kg$^{-1}$ of 0.5% isobaric bupivacaine (Aguettant, Lyon, France). The use of intrathecal (IT) clonidine 1 µg kg$^{-1}$ (Boehringer Ingelheim, Reims, France) as spinal anaesthesia adjuvant was left to the discretion of the anaesthetist according to his practice and the expected duration of surgery. Therapies used and intervention performed for the management of intraoperative events were left to the discretion of the anaesthetist. The monitoring of cerebral oxygen saturation by NIRS was achieved using INVOS™ Cerebral/Somatic Oximeter (COVİDIEN, Boulder, CO, USA). The screen monitor allowed continuous recording and real-time access of $S_cO_2$ values.

The following parameters were prospectively collected: patient characteristic data (birth term (week’s PMA), current adjusted age (week’s PMA), birth weight (kg), current weight (kg)), the nature of the planned surgery and preoperative haemoglobin level. Cardio-respiratory parameters (MAP, HR, and $Sp_O_2$) were recorded before any stimulation, in quiet setting and ambient air. All technical adverse events (haematomas, total spinal block, failure) and the need to modify anaesthetic management were also noted. Haemoglobin reference data were from the routine preoperative blood test collected before surgery.

We considered any reduction of over 10% of the $S_cO_2$ baseline as a clinically significant warning threshold. A decrease of more than 20% from reference value defined cerebral desaturation. Significant hypotension and reduction in HR were defined as a decrease of 20% or more from the reference value. $Sp_O_2$, less than 90% characterized a systemic desaturation.

**Statistics**

Analyses were based on a non-inferiority test with the primary hypothesis that the $S_cO_2$, at 15 and 30 min after SA would not differ from the reference value. We assumed a clinically significant variation as a decrease of over 10% of the $S_cO_2$ baseline. For MAP and HR, any decrease over 20% compared with the reference value was considered significant. To compare intraoperative values to the reference (T0), we used T15 and T30 values: T15...
value was defined as the lowest value measured during the first 15 min after the injection of the RA. The T30 value was the lowest value measured during the following 15 min. Relative variations of the rScO2, MAP and HR were calculated according the following formula:

$$VR(T15 \text{ or } T30) = \frac{|T(T15 \text{ or } T30) - T0|}{T0}$$

To evaluate the effectiveness of cerebral auto-regulation, a correlation (r) between changes in MAP and those of the rScO2 was searched using Spearman test. A strong correlation (r close to 1) reflects a lack of CA (rScO2 directly dependent on BP). Conversely, a low correlation (r close to 0) shows that variations of rScO2 and BP changes are independent.

The impact of a preterm birth (<37 weeks’ PMA) and IT clonidine adjunction on haemodynamic parameters and rScO2 variations were also analysed. Categorical data are summarized using counts and percentages, and continuous data using means (standard deviation) and median [interquartile range]. For comparisons between two groups, we used the parametric Student’s t-test or the nonparametric Mann-Whitney U-test according to normality of the variables. For comparisons of more than two groups, ANOVA or Kruskal-Wallis test (with Bonferroni correction) were used. A test was considered significant when P value was below the significant threshold of 5%.

Statistical analysis was performed in collaboration with the Medical Information department of Montpellier University Hospital using SAS software, SAS Institute Inc.

Results

In the two yr period, 116 children were recruited in the study. As detailed in the flowchart (Fig. 1), 13 patients were excluded because of missing data or failure of SA and 103 were included in the analysis. At the time of surgery, the median weight was 3680 g [2860 – 4200] and the median adjusted age was 43 weeks’ PMA [40–45.7]. Table 1 summarizes patient characteristic and surgical data.

Mean relative variations of rScO2 were −2.25% (97.5% CI [−3.97; −0.5]) at T15 and +0.11% (97.5% CI [−1.67; +1.90]) at T30. No significant rScO2 variation was detected over the 30 min after the SA. Mean relative variations of MAP at T15 and T30 were respectively −13.94% (97.5% CI [−17.74; −10.14]) and −20.27% (97.5% CI [−24.25; −16.29]). At T30, the 20% reduction threshold was exceeded, indicating a significant decrease in MAP. Mean variation in HR were −4.26% (97.5% CI [−6.81; −1.72]) at T15 and −12.69% (97.5% CI [−15.21; −10.17]) at T30 without significant change. Table 2 summarizes medians of MAP, rScO2 and HR measures at T0, T15 and T30 min after SA punctures. No correlation was detected between BP and rScO2 variations during 30 min after the SA (correlation coefficient: r = 0.085; P=0.38).

Subgroup analysis: intrathecal “IT Clonidine” or “No Clonidine”

Fifty-three patients received SA with addition of IT clonidine and 50 without. There were no patient characteristic differences between subgroups receiving IT clonidine or not, apart from a larger proportion of bilateral inguinal hernia repair in the “IT Clonidine” group. Within each groups, mean rScO2 were similar between T0, T15 and T30. No significant difference was detected in the mean rScO2 relative variations between the two compared groups. At T30, the MAP reduction was statistically higher in the “IT Clonidine” group. The relative rScO2 and MAP changes are represented in Fig. 2.
Among the 103 patients analysed, 17 infants presented an episode of rScO₂ decrease of more than 10% from their reference values ranging from –10% to –26.45%. Among them, 10/17 (57%) reported a concomitant significant decrease in MAP. 7/17 (41%) received IT clonidine and 8/17 (47%) were ex-preterm infants. Finally, 4 patients presented a cerebral desaturation with a decrease of more than 20%. None of these 4 events of cerebral desaturation exceeded fifteen min of duration and two out of four were associated with a significant decrease in MAP (–30 and –24% from the reference values).

**Adverse events related to spinal anaesthesia**

Four infants required conversion to general anaesthesia or supplemental sedation as a result of failure or insufficient spinal block and were excluded from the analysis. Two (1.7%) severe complications were noted (1 total spinal block and 1 episode of seizure) without any sequelae detected in postoperative period. Finally, no systemic desaturation SpO₂<90% was detected.

**Discussion**

The results of this study show that spinal anaesthesia is not associated with a significant decrease in rScO₂. Despite a clinically relevant decrease in MAP, the cerebral perfusion based on near infrared spectroscopy oximetry monitoring, remained highly stable. With the degree of BP variation reported in this work, the lack of correlation between changes in MAP and rScO₂ suggest an effective cerebral auto-regulation in infants under SA. The addition of IT clonidine or a preterm birth did not have any impact on these results.

Previously, Bonnet and colleagues⁵ postulated that cerebral perfusion could be altered in preterm infants after performing SA: they reported a reduction in arterial BP and consequent decrease in cerebral blood flow measured by transcranial Doppler. In our study, we used cerebral oximetry, which has been highly correlated with oxygen saturation of venous blood (SvO₂), an indirect measure of the balance between cerebral perfusion and brain metabolism requirements. Based on the clinical data published in paediatric cardiovascular surgery⁶ and in adult surgery,⁷,⁸ there is a correlation between major variations rScO₂ and poor perioperative neurological outcome. In contrast to the findings of Bonnet and colleagues no alteration in brain oxygenation measured by near infrared spectroscopy oximetry was found in infants over 30 min after SA puncture.

In children under five yr old, including neonates, it is commonly accepted that the haemodynamic consequences of SA remain low⁹–¹¹ related to the lower venous capacitance, the lower sympathetic tonus, the poor predictability of the upper level of the SA and the negative feedback on parasympathetic tone related to sympathetic block induced by SA.¹⁵,¹⁶ However, Bonnet and colleagues reported clinically relevant variations of MAP (mean decrease in MAP>20%) after SA in former preterm infants. Similarly, hypotension reported in the current study appeared greater than variations previously described in trials using low doses of tetracaine and vasopressors to extend the duration of the block.¹⁴ In our practice, isobaric bupivacaine at the dose of 1 mg kg⁻¹ and intrathecal clonidine may also explain a part of these differences. In this work, the use of clonidine was associated with statistically significant MAP decrease compared with the group without IT clonidine (~26.62% vs ~13.66%; P=0.001). However, no significant change in brain oxygen saturations was noted. At the dose of 1 µg kg⁻¹, this result confirms the safety of IT clonidine use in infants.¹⁶ A history of prematurity has been described as a risk factor for hypotension after SA.⁹,¹⁷ In contrast, our results showed no difference in MAP variations between subgroups of former preterm and term neonates.
The role of hypotension in the genesis of stroke occurring in the neonatal period is still controversial. Recent literature confirms a potentially deleterious impact of severe haemodynamic variability in the neonatal period with a strong association between hypotension and poor neurological outcome. This raises numerous questions about the efficiency of cerebral auto-regulation in neonates. Animal experimental data found an effective CA in newborn lamb and piglet models.
10% of reference value. All these events were brief and isolated. Patients had a decrease in cerebral saturation value above the related to cerebral desaturation: however, we observed that 17 studies were not designed to analyse population and therapeutic action sufficient to guarantee the reliability of our results. The study was therefore based on clinical and surgical criteria that did not including in the former preterm.

Some limits may be discussed: this study was observational. However, calculation of the number of subjects required (NSN) constitutes an important methodological aspect to consider. Thus, a calculation of the NSN, has been achieved: a post-hoc power of 90%, the NSN was estimated at 81

<table>
<thead>
<tr>
<th>Term birth</th>
<th>IT Clonidine</th>
<th>No Clonidine</th>
<th>Preterm birth</th>
<th>IT Clonidine</th>
<th>No Clonidine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 27</td>
<td>N = 25</td>
<td></td>
<td>N = 25</td>
<td>N = 26</td>
</tr>
<tr>
<td>rSO2 (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>71 [68; 81]</td>
<td>71 [66; 77]</td>
<td>71.5 [69; 77]</td>
<td>70 [66; 73]</td>
<td></td>
</tr>
<tr>
<td>T15</td>
<td>71 [63.5; 77]</td>
<td>70.5 [67; 76]</td>
<td>73 [67; 79]</td>
<td>67.5 [63; 74]</td>
<td></td>
</tr>
<tr>
<td>T30</td>
<td>72.5 [65; 79.5]</td>
<td>71 [67.5; 77]</td>
<td>74.5 [67.5; 79]</td>
<td>71.5 [65.5; 75]</td>
<td></td>
</tr>
<tr>
<td>VR T30</td>
<td>0 [-9; 3.3]</td>
<td>0.7 [-4.6; 7.6]</td>
<td>1.6 [-3.5; 8.5]</td>
<td>-0.9 [-5.4; 3]</td>
<td></td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>63 [57; 74]</td>
<td>70 [62; 78]</td>
<td>60 [56; 71]</td>
<td>64 [53; 74.5]</td>
<td></td>
</tr>
<tr>
<td>T15</td>
<td>55 [48.5; 64]</td>
<td>59 [52; 67.5]</td>
<td>48 [42; 51]</td>
<td>54 [47; 60.5]</td>
<td></td>
</tr>
<tr>
<td>T30</td>
<td>45 [41; 52]</td>
<td>57 [48; 63]</td>
<td>43 [40; 47.5]</td>
<td>50.5 [46; 54.5]</td>
<td></td>
</tr>
<tr>
<td>VR T30</td>
<td>-32 [-38; -19]</td>
<td>-18 [-28.5; -1.5]</td>
<td>-25 [-35; -25.5]</td>
<td>-16 [-31; -1.5]</td>
<td></td>
</tr>
<tr>
<td>HR (beats min⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>180 [160; 192]</td>
<td>170 [145; 185]</td>
<td>167 [155; 190]</td>
<td>171 [160; 187]</td>
<td></td>
</tr>
<tr>
<td>T15</td>
<td>164 [140; 180]</td>
<td>171 [152; 175]</td>
<td>153 [144; 174]</td>
<td>167 [151; 182]</td>
<td></td>
</tr>
<tr>
<td>T30</td>
<td>142 [130; 165]</td>
<td>149 [144; 170]</td>
<td>147 [133; 155]</td>
<td>152 [160; 169]</td>
<td></td>
</tr>
<tr>
<td>VR T30</td>
<td>-17 [-27; -9.5]</td>
<td>-7 [-16; 4.5]</td>
<td>-12 [-19; -10.5]</td>
<td>-14 [-23; -3]</td>
<td></td>
</tr>
</tbody>
</table>

Neither a significant MAP decrease (more than 20%), nor IT clonidine and prematurity appeared to be associated with these cases of cerebral saturation decrease. A more precise study of this subgroup could have looked for an auto-regulation threshold and for risk factors of cerebral desaturation. The small size of this subgroup did not allow us to carry out this analysis. The lack of randomization is another bias to consider in result interpretation. First, the use of clonidine was left to the choice of the anaesthesiasts, with a main objective to extend the duration of SA when surgery might exceed the assumed length of the spinal anaesthetic block. Bilateral inguinal hernia repair was then the major indicator of IT clonidine. The choice of adding clonidine was therefore based on clinical and surgical criteria that did not allow randomization. Secondly, to assess whether the choice of anaesthetic technique had an influence on cerebral oximetry during neonatal surgery, SA could have been compared with general anaesthesia. For many yr, in our unit of paediatric anaesthesia, spinal anaesthesia has been widely studied and remains currently our first choice for all sub-umbilical in- fant surgeries shorter than 90 min duration. This practice is supported by a decreased risk of postoperative apnoea and avoidance of all exposure to the potential neurotoxicity of inhaled and systemic anaesthetic agents, both remain strong arguments in favour of spinal anaesthesia. Previous epidemiological reports have shown the safety and efficacy of this technique. In accordance, we report in our cohort, a success rate over 95% and an absence of respiratory complications. Finally, in accordance with our local protocol, all neonates were pre-treated with intra-rectal atropine. This practice is not standard of care for all paediatric institutions caring for young infants and may have impacted the BP and HR variability.

**Conclusion**

Spinal anaesthesia did not cause significant decrease in cerebral oxygen saturation even among former preterm and when using...
IT clonidine. Within the limits of MAP variations reported in this study, cerebral auto-regulation seems present and remains effective after SA in former preterm or full term infants.

**Authors’ contributions**

Study design/planning: C.S., L.H., S.B., O.R., C.D.  
Data analysis: S.B.  
Writing paper: C.S., L.H., S.D.M.  
Revising paper: all authors

**Declaration of interest**

None declared.

**Funding**

Support was provided solely from institutional and departmental sources of Lapeyronie University Hospital, Montpellier, France.

**References**

study—comparing apnea and neurodevelopmental outcomes, a randomized controlled trial. *Anesthesiology* 2015; 123:38–54


*Handling editor: Anthony R. Absalom*